Down-regulation of brain-pancreas relative protein in diabetic rats and by high glucose in PC12 cells: prevention by calpain inhibitors

Lu Tie and Xuejun Li
Department of Pharmacology, School of Basic Medical Sciences, Peking University, 38 Xueyuan Road, Haidian District, Beijing, 100191 Beijing, China
tielu@bjmu.edu.cn

Brain-Pancreas Relative Protein (BPRP) is a novel protein found in our laboratory. Previously we demonstrated that it is involved in ischemia and depression. In light of the putative association between diabetes and clinical depression, and the selective expression of BPRP in brain and pancreas, we examined in this study whether BPRP levels are affected by induction of diabetes by alloxan injection in rats and exposure to high glucose levels in PC12 cells. Western blot and immunohistochemical analyses revealed that BPRP levels were decreased in the hippocampal CA1 neurons of diabetic rats 4 and 8 weeks post-alloxan injection and in PC12 cells 48 h after exposure to high concentrations of glucose. BPRP protein levels were not affected by osmolarity control treatments with mannitol. Follow-up pharmacological experiments in PC12 cells revealed that glucose-induced BPRP down-regulation was markedly attenuated by the calpain inhibitors N-acetyl-Leu-Leu-Norleucinal (ALLN) or calpeptin, but not the proteasome-specific inhibitor carbobenzoxy-Leu-Leu-Leucinal (MG132). The ability of calpain inhibitors to specifically counter the effects of high glucose exposure on BPRP levels further suggests that BPRP and calpain activity may contribute diabetes complications in the central nervous system.